UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/662,757	09/15/2003	Michael S. Williams	9362-3	1920

20792 7590 02/12/2008
MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

EXAMINER	
LIN, JAMES	

ART UNIT	PAPER NUMBER
1792	

MAIL DATE	DELIVERY MODE
02/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/662,757	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Jimmy Lin	1792	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *73-104* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *73-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 73-74, 76, 80-84, and 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Igaki et al. (WO 2002/43799, references made are to the English equivalent U.S. Publication No. 2003/0104030). (The statement of rejection has been changed to correct an obvious typographical error. Specifically, Guruwaiya et al. (U.S. Patent No. 6,251,136) was removed from the statement of rejection since Guruwaiya was obviously not mentioned in the grounds of rejection, much less used for its teachings.)

Igaki discloses a method of impregnating a stent with a pharmacological agent (abstract), the method comprising:

immersing a stent comprising a polymeric material in a mixture of a carrier fluid and a pharmacological agent [0052];

pressurizing the mixture of carrier fluid and pharmacological agent for a time sufficient to cause the carrier fluid and pharmacological agent to at least partially penetrate the polymeric material [0057];

removing the pressure such that the carrier fluid diffuses out of the polymeric material [0062] and such that an amount of the pharmacological agent remains elutably trapped within the polymeric material [0011].

The polymeric layer is only a single layer and, thus, is interpreted to be a non-layered polymeric material.

Igaki teaches that the removal of the pressure involves the opening of a valve to gradually exhaust the carrier fluid [0062], but does not explicitly teach that the pharmacological agent becomes elutably trapped within the polymeric material in a predetermined concentration gradient due to the removal of the pressure under controlled conditions. However, Igaki teaches

that the pressure is gradually exhausted (i.e., removing the pressure over a predetermined period of time) in a reaction chamber (i.e., under controlled conditions) and, thus, teaches all the steps as claimed. Because the method of Igaki is so similar to the claimed steps, the two methods must necessarily achieve similar results. Unless critical steps are missing from the claims, the pharmacological agent must necessarily have some sort of concentration gradient within the polymeric material in the method of Igaki. This concentration gradient, therefore, must necessarily define an elution profile of the pharmacological agent, as required in the claims. Additionally, the predetermined concentration gradient can be zero.

Claim 74: The pressure and rate of pressure change is controlled during the step of removing the pressure.

Claims 76,80: Supercritical carbon dioxide is the carrier fluid [0052]-[0058].

Claims 81,83: The carbon dioxide can contain a co-solvent, such as ethanol [0053].

Claim 82: The carrier fluid is used to cause the polymer to become swollen [0063], thereby altering the diffusion coefficients of the polymeric material.

Claim 84: The intraluminal prosthesis is a stent (abstract).

Claim 86: The polymeric material can be formed only on the surface of the stent.

3. Claims 75, 99-101, and 104 are rejected under 35 U.S.C. 103(a) as being unpatentable over Igaki '799 in view of Guruwaiya et al. (U.S. Patent No. 6,251,136).

Igaki is discussed above, but does not explicitly teach the step of masking the stent. However, Guruwaiya teaches a method of coating a pharmacological agent on a stent (abstract), wherein certain portions of the stent are masked during the coating process. The mask is used to selectively coat the stent in order to achieve a specific effect when using the stent for its intended purpose (col. 2, lines 49-66). Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to have masked certain portions of the stent of Igaki with a reasonable expectation of success. One would have been motivated to do so in order to have achieved a specific effect as described in Guruwaiya. The mask is then removed after the coating of the pharmacological agent because the mask is not part of the final product.

Claim 99: Guruwaiya teaches that two different portions of the stent can be coated with two different pharmacological agents (col. 4, lines 58-62), thus requiring a first masking step to

apply the first pharmacological agent and a second masking step to apply the second pharmacological agent. Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to have masked first and second portions and to have applied a first and second pharmacological agent to the unmasked regions of Igaki in order to have manufactured a stent having two different effects.

Claim 100: Igaki teaches that the pressure and rate of pressure change is controlled during the step of removing the pressure.

Claims 101,104: Igaki teaches that the carrier fluid can be supercritical carbon dioxide.

4. Claims 73-74, 76-78, 80-82, 86, 88-89, 91-93, and 98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greiner (EP 0405284, of record as listed by the Applicant).

Greiner teaches a method of impregnating a catheter with a pharmacological agent (col. 2, lines 33-35). The catheter is placed in a pressure vessel. The pharmacological agent is added to the reactor and carbon dioxide (i.e., a carrier fluid) is used to pressurize the reactor. The reactor is then cooled and depressurized (Example 1). The pharmacological agent has at least partially penetrated and become impregnated into the polymeric material (col. 3, lines 23-27). The polymeric material forms a single layer and, thus, is interpreted to be a non-layered polymeric material.

The polymeric material would necessarily have a concentration gradient of the pharmacological agent for substantially the same reasons as discussed above. Additionally, the predetermined concentration gradient can be zero gradient.

Claims 77-78,81,88,93: Greiner does not explicitly teach that the reactor is pressurized with an inert gas consisting of helium, nitrogen, and argon. However, Greiner does exemplify both carbon dioxide and nitrogen as preferred and suitable carrier fluids (col. 3, lines 12-22). One of ordinary skill in the art would have expected that using a combination of suitable carrier fluids (i.e., using both carbon dioxide and nitrogen) as taught by Greiner to have similar results as just using carbon dioxide alone. Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to have used carbon dioxide along with nitrogen gas, instead of just using carbon dioxide alone, in the method of Greiner with a reasonable expectation of success because Greiner teaches that both gases are suitable carrier fluids and

because one of ordinary skill in the art would have expected similar results when using a combination of carrier fluids as opposed to using only a single carrier fluid.

Claims 74,89: The pressure is lowered in the reactor (col. 4, lines 2-6). There must be some control of how fast the rate of pressure changes.

Claims 76,80,91-92: The carrier fluid can be supercritical carbon dioxide (col. 3, lines 12-27).

Claim 82: The supercritical carbon dioxide causes the intraluminal prothesis to swell, thereby causing a more complete diffusion of the pharmacological agent (col. 3, lines 23-29).

Claims 86 and 98: The polymeric material can be formed only on the surface.

5. Claims 75, 90, and 99-104 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greiner '284 as applied to claim 78 above, in view of Guruwaiya '136.

Greiner is discussed above, but does not explicitly teach the step of masking the catheter. However, such would have been obvious over Guruwaiya for substantially the same reasons as discussed above.

Claim 99 is rejected for substantially the same reasons as discussed in the rejection over Igaki '799 in view of Guruwaiya '136.

6. Claim 79 is rejected under 35 U.S.C. 103(a) as being unpatentable over Igaki '799 as applied to claim 73 above, and further in view of Edwards et al. (U.S. Patent 6,670,398).

Igaki is discussed above, but does not teach the use of everolimus as the pharmacological agent. However, Edwards teaches everolimus is a therapeutic drug that can be used to suppress the transplant recipient's immune response against the transplanted organ or tissue (col. 2, lines 3-10). Everolimus can be coated onto a stent (col. 21, lines 8-39). The selection of something based on its known suitability for its intended use has been held to support a prima facie case of obviousness. Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945). Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to have impregnated everolimus as the particular pharmacological agent onto the stent of Igaki with a reasonable expectation of success because Edwards teaches that it is suitable to administer

everolimus using a stent and because one would have been motivated to do so in order to provide stent for use in organ or tissue transplant.

7. Claims 79 and 95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greiner '284 as applied to claims 73 and 88 above, and further in view of Edwards '398 for substantially the same reasons as discussed immediately above.

8. Claims 85 and 97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greiner '284 as applied to claim 73 above, and further in view of Mehta et al. (WO 01/87368).

Greiner is discussed above, but does not explicitly teach the polymeric material can be non-erodible. However, Greiner does teach the desire to control the release of the drug into the target site (col. 4, lines 39-41). Mehta teaches a method of making a stent, wherein the stent is coated with a polymer and a pharmacological agent (pg. 7, lines 12-29). The polymeric material can be either biostable (i.e., non-erodible) or bioabsorbable (i.e., erodible) depending on the desired rate of release (pg. 8, lines 9-22). Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to have used a biostable polymer in the process of making the stent of Greiner. One would have been motivated to do so in order to have controlled the rate of release of the pharmacological agent.

9. Claim 87 is rejected under 35 U.S.C. 103(a) as being unpatentable over Igaki '799 as applied to claim 73 above, and further in view of Ragheb et al. (U.S. Patent 6,299,604).

Igaki and Guruwaiya are discussed above. Igaki teaches herapin as an example of a pharmacological agent [0050], but does not explicitly teach using a radiopaque material. However, Ragheb teaches that a radiopaque material is a suitable alternative to herapin for use in the vascular system. The selection of something based on its known suitability for its intended use has been held to support a prima facie case of obviousness. Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945). Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to have used a radiopaque material as the particular pharmacological agent with a reasonable expectation of success because Ragheb

teaches that radiopaque materials are suitable pharmacological agents that can be used in the vascular system.

10. Claim 87 is rejected under 35 U.S.C. 103(a) as being unpatentable over Greiner '284 as applied to claim 73 above, and further in view of Ragheb '604 for substantially the same reasons as discussed immediately above.

11. Claims 81, 83-84, 86, 93-94, 96, and 98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greiner '284 as applied to claims 88 above, and further in view Igaki '799.

Claims 81,83,93-94: Greiner is discussed above, but does not explicitly teach that a co-solvent consisting of the group of ethanol and methanol can be used with the carbon dioxide. However, Igaki teaches that a co-solvent such as ethanol can be added to the carbon dioxide to increase the impregnation of the pharmacological agent [0053]. Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to have added ethanol to the carbon dioxide of Greiner with a reasonable expectation of success. One would have been motivated to do so in order to have increased the impregnation of the pharmacological agent.

Claims 84,86,96,98: Greiner does not explicitly teach that the intraluminal prothesis can be used as a stent. Greiner only teaches that above-discussed method can be used for a catheter. However, Igaki teaches a similar process for impregnating a stent for similar purposes and, thus, one of ordinary skill in the art would have expected similar results for impregnating a stent as compared to impregnating a catheter. Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to have impregnated a stent, as opposed to a catheter, using the method of Greiner with a reasonable expectation of success because Igaki teaches a similar process can be performed on stents to achieve similar results.

Response to Arguments

12. Applicant's arguments filed 12/3/2007 have been fully considered but they are not persuasive.

Applicant argues on pg. 10 that one skill in the art would not, upon reading Igaki, produce a non-layered stent with a drug concentration gradient in the stent material. However,

the does not requires a non-layered stent, but merely a non-layered polymeric material. The formation of a single layer with the polymeric material has been interpreted to be a non-layered polymeric material. Both Igaki and Greiner teach that a polymeric material is used to form a single layer.

Applicant argues on pg. 10 that Igaki utilizes layers to control the time of drug release and the quantity of drug release and that Igaki does not utilize a drug concentration gradient for accomplishing time of drug release and/or quantity of drug release. However, Igaki teaches that the use of multiple layers is optional because multiple layers are used only "if it is necessary to meticulously control the release into the blood vessel" [0067]. Although the release of the drug is accomplished through degradation of the polymeric material, at least some of the impregnated drug will necessarily be released from the polymeric material prior to degradation of the polymeric material because Igaki and the present invention are so similar that similar results must necessarily occur.

Applicant argues on pg. 11 that Greiner fails to teach of suggest a drug elutably trapped within the polymeric material in a predetermined concentration gradient. However, Greiner does teach the lowering of pressure such that the carrier fluid is separated from the polymeric material and, thus, teaches all the active claimed steps. If Greiner is performing all the same steps as the claims, the same result must necessarily be achieved. Unless some critical steps are missing, the method of Igaki necessarily produces some sort of concentration gradient of the pharmacological agent in the polymeric material. Additionally, assuming *arguendo* that a concentration gradient is not formed, the predetermined concentration gradient can also include zero gradient because the term "predetermined" is not limited to any specific values.

13. Applicant's arguments, see pg. 16, filed 12/3/2007, with respect to claim 85 have been fully considered and are persuasive. The rejection of the claim over Igaki and Mehta has been withdrawn.

Conclusion

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Mehta et al. (U.S. Publication 2002/0051845) teaches a method of coating a stent with supercritical CO_2.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jimmy Lin whose telephone number is (571)272-8902. The examiner can normally be reached on Monday thru Friday 8AM - 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tim Meeks can be reached on 571-272-1423. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy H Meeks/
Supervisory Patent Examiner, Art Unit 1792

/Jimmy Lin/
Examiner, Art Unit 1792